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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/705,944 | 11/13/2003 | Xuri Li | 029065.48885D1 | 8302 |

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| EXAMINER | |
|---|---|
| YU, MISOOK | |
| **ART UNIT** | **PAPER NUMBER** |
| 1642 | |

| MAIL DATE | DELIVERY MODE |
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/705,944 | LI ET AL. | |
| | Examiner | Art Unit | |
| | MISOOK YU, Ph.D. | 1642 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *22 March 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *17-79* is/are pending in the application.

4a) Of the above claim(s) *17-49,56,58 and 61-79* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *51-55,57,59 and 60* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/13/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

### *Election/Restrictions*

Applicant's election with traverse of group V with FITC as the elected label in the reply filed on 3/22/2007 is acknowledged. The traversal is on the ground(s) that inventions IV, V, VI, and IX are linked by an inventive concept of isoform-specific VEGF-B antibodies their uses, therefore searching the antibody would necessarily uncover the art related to uses of antibodies. This is not found persuasive because groups IV, VI, and IX are different methods of using the antibodies and searching different method of using the antibody require different search, which requires serious burden on the examiner.

The requirement is still deemed proper and is therefore made FINAL.

Claims 17-50 and 61-79 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, and claims 56 and 58 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected species, there being no allowable generic or linking claim.

Claims 17-79 are pending and claims 51-55, 57, 59, and 60 are examined on merits.

### *Claim Rejections - 35 USC § 101*

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

the claimed invention is directed to non-statutory subject matter. Claim 51 as written, does not sufficiently distinguish over antibodies as they exist naturally because the

claims do not particularly point out any non-naturally occurring differences between the claimed products and the naturally occurring products. In the absence of the hand of man, the naturally occurring products are considered non-statutory subject matter. *See Diamond v. Chakrabarty*, 447 U.S. 303, 206 USPQ 193 (1980). The claims should be amended to indicate the hand of the inventor, e.g., by insertion of "Isolated" or "Purified". See MPEP 2105.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 51, 55, and 57 are rejected under 35 U.S.C. 102(b) as being anticipated by Salven et al (1998, Am. J. Pathology, vol., 153, pages 103-8).

Claims 51, 55, and 57 are drawn to antibody specific for VEGF-B186, but not VEGF-B187, wherein the antibody is covalently or noncovalently labeled in claim 55, and labeled with various art-used labels in claim 57.

Salven et al., teach at page 104, right column, under the heading "*immunohistochemistry*" a VEGF-B186 specific antibody.

The Office does not have the facilities and resources to provide the factual evidence needed in order to establish that the VEGF-B186 specific antibody binds to VEGF-B187. This determination requires laboratory work. In the absence of evidence to the contrary, the burden is on the applicant to prove that the VEGF-B186 specific

antibody reacts with VEGF-B187. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 51-55, 57, and 60 are rejected under 35 U.S.C. 103(a) as being unpatentable over Salven et al (IDS, 1998, Am. J. Pathology, vol., 153, pages 103-8) in view of Campbell, A. (1986, Monoclonal antibody technology, chapter 1 only, Elsevier Science Publishers B.V., Netherlands).

Claims 51-55, 57, 59, and 60 are drawn to antibody specific for VEGF-B186, but not VEGF-B187, wherein the antibody is monoclonal (claim 52), humanized (claim 53), chimeric (claim 54), covalently or noncovalently labeled in claim 55, and labeled with various art-used labels in claim 57, labeled with FITC in claim, and in pharmaceutically acceptable excipient in claim 60.

Salven et al., teach at page 104, right column, under the heading "*immunohistochemistry*" a VEGF-B186 protein.

Salven et al., do not teach monoclonal antibody, and the various labels. However, Campbell, A. teaches that making and screening monoclonal antibodies binding to specific epitopes are a routine matter at the current state of antibody art (see Table 1.1 at page 5) and one of ordinary skill in the art is motivated to make antibody for

various reasons (see the last paragraph of page 29). Therefore, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to make an antibody and/or monoclonal antibody capable of binding to VEGF-B186, but not VEGF-B187, especially given Salven et al., teach many different VEGF isoforms are involved in cancer development. As for label, human antibody, and chimeric antibody, Campbell, A teaches attaching label to antibody and making chimeric and human antibody were known in the art before the effective filing date of the instant application. See page 19. As for pharmaceutically acceptable expedient, Campbell, A at page 20 teach that antibody, especially monoclonal antibodies had been used for therapeutic uses and one of skill in the art would be able to mix the antibody in a pharmaceutically acceptable excipient.

Further, the Board of Patent Appeals and interferences has taken the position that once an antigen has been isolated, the manufacture of antibodies against it is *prima facie* obvious. See Ex parte Erlich 22 USPQ2d 1463 (BdPatApp&Int 1992).

Claim 51, 55, 57, and 59 are rejected under 35 U.S.C. 103(a) as being unpatentable over Salven et al (1998, Am. J. Pathology, vol., 153, pages 103-8) in view of Campbell, A. (1986, Monoclonal antibody technology, chapter 1 only, Elsevier Science Publishers B.V., Netherlands), and in further in view of US 6,025,194 (filed in 1997).

Claim 59 not rejected above is drawn to antibody labeled with FITC, and US 6,025,194 teaches that labeling an antibody with FITC had been well known before the

effective filing date of the instant application. Therefore it would have been obvious to one of skill in the art to make and use the claimed invention with a reasonable expectation of success.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MISOOK YU, Ph.D. whose telephone number is 571-272-0839. The examiner can normally be reached on 8 A.M. to 5:30 P.M., every other Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shanon Foley can be reached on 571-272-0898. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

MISOOK YU, Ph.D.
Primary Examiner
Art Unit 1642

/Misook Yu/